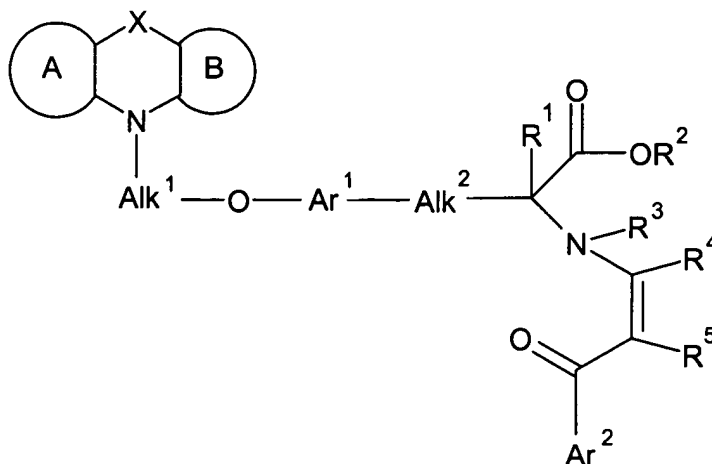


WHAT IS CLAIMED IS:

1. A compound of Formula I



(I)

wherein

ring A and ring B, fused to the ring containing X and N, independently of each other represents a 5-6 membered cyclic ring, which may optionally contain one or more

- heteroatoms selected from oxygen, sulfur or nitrogen atoms and may optionally substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; the ring A and ring B may be saturated or contain one or more double bonds or may be aromatic;

X is a valence bond, CH₂CH₂, CH=CH, O, S, or NR⁶ wherein R⁶ represents H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

- R¹ is H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

R² is H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R³ is H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or

heteroaryl;

R^4 and R^5 are independently H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; R^4 and R^5 may form a 5 or 6 membered ring optionally substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

Alk^1 represents C_{1-6} alkylene;

Alk^2 represents C_{1-2} alkylene;

Ar^1 represents arylene, hetero arylene, or a divalent heterocyclic group optionally substituted with one or more halogen, C_{1-6} alkyl, amino, hydroxy, C_{1-6} alkoxyl or aryl.

Ar^2 represents an aryl group substituted with none, one or more halogen, C_{1-6} alkyl, amino, hydroxy, C_{1-6} alkoxyl or aryl; a hetero aryl, or a heterocyclic group optionally substituted with one or more halogen, C_{1-6} alkyl, amino, hydroxy, C_{1-6} alkoxyl or aryl.

2. A compound according to claim 1, wherein

ring A is a 6 membered aromatic ring;

ring B is a 6 membered aromatic ring;

X is a valence bond, CH_2CH_2 , $CH=CH$, O or S;

R^1 is H or alkyl;

R^2 is H or alkyl;

R^3 is H or alkyl;

R^4 and R^5 are independently H or alkyl;

Alk^1 is C_{2-3} alkylene;

Alk^2 is C_{1-2} alkylene;

Ar^1 is an arylene group

Ar^2 is a substituted aryl group.

3. A compound according to claim 1, wherein
 ring A is a 6 membered aromatic ring;
 ring B is a 6 membered aromatic ring;
 X is a valence bond, CH₂CH₂, CH=CH, O or S;
 5 R¹ is H or alkyl;
 R² is H or alkyl;
 R³ is H or alkyl;
 R⁴ and R⁵ form a 6 membered aromatic ring;
 Alk¹ is C₂₋₃alkylene;
 10 Alk² is C₁₋₂alkylene;
 Ar¹ is 6 membered aromatic ring
 Ar² is a substituted aryl group.
4. A compound according to claim 1, wherein
 15 ring A is a benzene ring;
 ring B is a benzene ring;
 X is a valence bond, CH₂CH₂, CH=CH, O or S;
 R¹ is H;
 R² is H;
 20 R³ is H;
 R⁴ is methyl; R⁵ is H;
 Alk¹ is CH₂CH₂;
 Alk² is CH₂;
 Ar¹ is benzene ring;
 25 Ar² is benzene ring substituted with none, one or more fluorine;

5. A compound according to claim 1, wherein
 ring A is a benzene ring;
 ring B is a benzene ring;
 X is a valence bond, CH₂CH₂, CH=CH, O or S;
- 5 R¹ is H;
 R² is H;
 R³ is H;
 R⁴ and R⁵ form a benzene ring;
 Alk¹ is CH₂CH₂;
- 10 Alk² is CH₂;
 Ar¹ is benzene ring;
 Ar² is benzene ring substituted with none, one or more fluorine;
6. A compound according to claim 1, wherein
- 15 ring A is a benzene ring;
 ring B is a benzene ring;
 X is a valence bond, CH₂CH₂, CH=CH, O or S;
 R¹ is H;
 R² is H;
- 20 R³ is H;
 R⁴ is methyl; R⁵ is H;
 Alk¹ is CH₂CH₂;
 Alk² is CH₂;
 Ar¹ is benzene ring;
- 25 Ar² is pyridine ring substituted with none, one or more halogen.

7. A compound according to claim 1, wherein
- ring A is a benzene ring;
- ring B is a benzene ring;
- X is a valence bond, CH_2CH_2 , $\text{CH}=\text{CH}$, O or S;

5 R^1 is H;

 R^2 is H; R^3 is H;

R^4 and R^5 form a benzene ring;

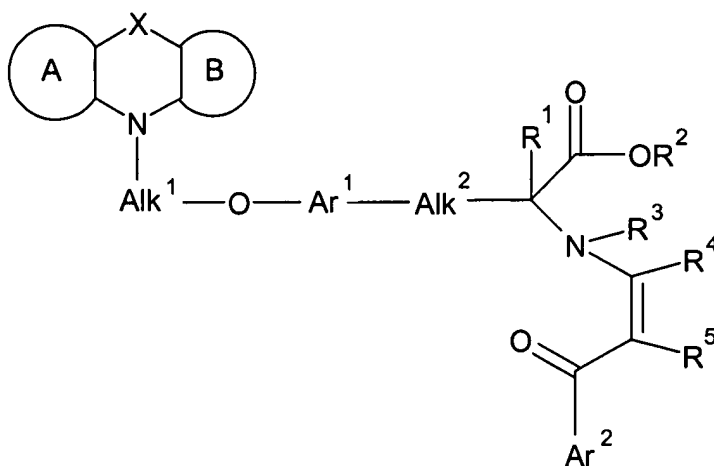
Alk¹ is CH₂CH₂;

10 Alk^2 is CH_2 ;

Ar¹ is benzene ring;

Ar² is pyridine ring substituted with none, one or more fluorine.

8. A process for the preparation of a compound of Formula I



(I)

20 wherein

ring A and ring B, fused to the ring containing X and N, independently of each other represents a 5-6 membered cyclic ring, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen atoms and may optionally substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl,

heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; the ring A and ring B may be saturated or contain one or more double bonds or may be aromatic;

5 X is a valence bond, CH₂CH₂, CH=CH, O, S, or NR⁶ wherein R⁶ represents H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R¹ is H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino,
10 alkylamino, arylamino, or aralkylamino;

R² is H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R³ is H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

15 R⁴ and R⁵ are independently H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; R⁴ and R⁵ may form a 5 or 6 membered ring optionally substituted with one or more halogen, hydroxy, nitro, cyano, alkyl,
20 alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

Alk¹ represents C₁₋₆alkylene;

25 Alk² represents C₁₋₂alkylene;

Ar¹ represents arylene, hetero arylene, or a divalent heterocyclic group optionally substituted with one or more halogen, C1-6alkyl, amino, hydroxy, C1-6alkoxyl or aryl.

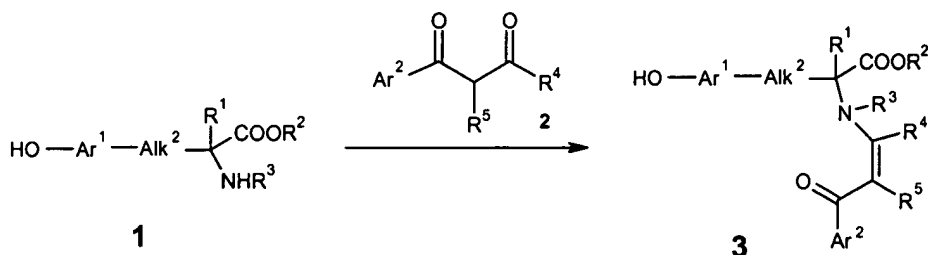
Ar² represents an aryl group substituted with none, one or more halogen, C1-6alkyl, amino, hydroxy, C1-6alkoxyl or aryl; a hetero arylene, or a divalent heterocyclic group
30 optionally substituted with non, one or more halogen, C1-6alkyl, amino, hydroxy,

C1-6alkoxyl or aryl,

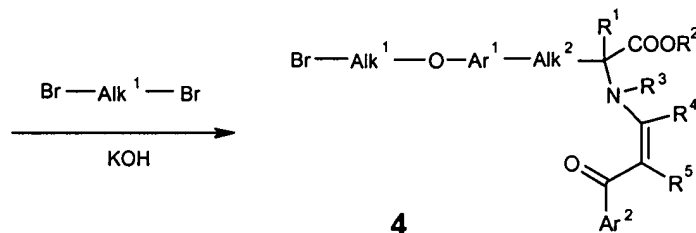
a stereoisomer, enantiomer, diastereomer, hydrate or pharmaceutically acceptable salts

thereof comprising the steps of:

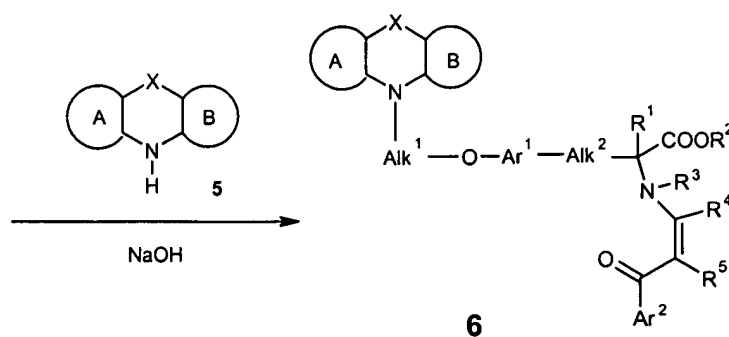
- a) initiating a condensation reaction between compound 1 and β -diketone 2 to give the
5 vinylogous amide analogues 3;



- b) performing O-Alkylation of 3 to gave compound 4;



- c) performing N-Alkylation of 4 gave the substituted arylalcanoic acid derivatives 6.



9. A process according to claim 8 wherein:

- (a) the condensation reaction is carried out in ethanol at reflux temperature;
(b) the O-alkylation is achieved by treatment of 3 with KOH and dibromoalkane in
20 ethanol;

(c) the N-alkylation is achieved by treating compound 4 with NaOH and compound 5 in the presence of tetrabutyl ammonium bromide.

10. A compound according to claim 1, wherein said compound is a PPAR pan agonist that
5 activates RXR/PPARalpha, RXR/PPARGamma, and RXR/PPARdelta heterodimers.

11. A compound according to claim 10, wherein said compound is a partial PPAR pan
agonist that activates RXR/PPARalpha, RXR/PPARGamma, and RXR/PPARdelta
heterodimers to differential extents.

10

12. A pharmaceutical composition for activating nuclear receptors comprising an effective
amount of a compound according to claim 1 or its pharmaceutically acceptable salt with at
least one pharmaceutically acceptable carrier or diluent.

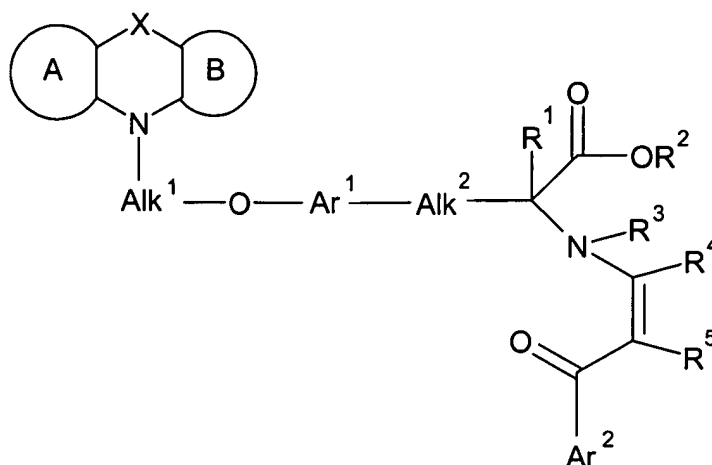
15 13. The pharmaceutical composition according to claim 11 wherein the nuclear receptors
comprise the Retinoid X Receptor (RXR) and the Peroxisome Proliferator-Activated
Receptors (PPAR).

14. The pharmaceutical composition of claim 12 in unit dosage form, comprising from about
20 0.05 to about 200 mg of the compound.

15. The pharmaceutical composition of claim 14 in unit dosage form, comprising from about
0.1 to about 100 mg of the compound

25 16. The pharmaceutical composition of claim 12 which is suitable for administration by an
oral, nasal, transdermal, pulmonary, or parenteral route.

17. A method of treating or preventing a condition mediated by at least one nuclear receptor, comprising administering to a subject in need thereof an effective amount of a compound of Formula I



(I)

wherein

ring A and ring B, fused to the ring containing X and N, independently of each other represents a 5-6 membered cyclic ring, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen atoms and may optionally substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; the ring A and ring B may be saturated or contain one or more double bonds or may be aromatic;

X is a valence bond, CH₂CH₂, CH=CH, O, S, or NR⁶ wherein R⁶ represents H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R¹ is H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

R² is H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R³ is H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R⁴ and R⁵ are independently H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; R⁴ and R⁵ may form a 5 or 6 membered ring optionally substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

Alk¹ represents C₁₋₆alkylene;

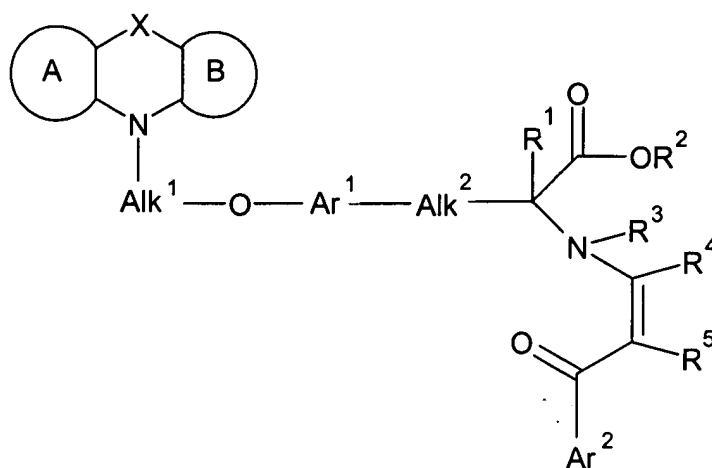
Alk² represents C₁₋₂alkylene;

Ar¹ represents arylene, hetero arylene, or a divalent heterocyclic group optionally substituted with one or more halogen, C₁₋₆alkyl, amino, hydroxy, C₁₋₆alkoxyl or aryl.

Ar² represents an aryl group substituted with none, one or more halogen, C₁₋₆alkyl, amino, hydroxy, C₁₋₆alkoxyl or aryl; a hetero aryl, or a heterocyclic group optionally substituted with one or more halogen, C₁₋₆alkyl, amino, hydroxy, C₁₋₆alkoxyl or aryl.

18. A method according to claim 17, wherein the nuclear receptors comprise a Retinoid X Receptor (RXR) and Peroxisome Proliferator-Activated Receptors (PPAR).

19. A method of treating or preventing a condition mediated by reduced activity of at least one nuclear receptor, comprising administration to a subject in need thereof an effective amount of a compound of Formula I



(I)

wherein

ring A and ring B, fused to the ring containing X and N, independently of each other represents a 5-6 membered cyclic ring, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen atoms and may optionally substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; the ring A and ring B may be saturated or contain one or more double bonds or may be aromatic;

X is a valence bond, CH₂CH₂, CH=CH, O, S, or NR⁶ wherein R⁶ represents H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R¹ is H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

R² is H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R³ is H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R⁴ and R⁵ are independently H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; R⁴ and R⁵ may form a 5 or 6 membered ring optionally substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

Alk¹ represents C₁₋₆alkylene;

Alk² represents C₁₋₂alkylene;

Ar¹ represents arylene, hetero arylene, or a divalent heterocyclic group optionally substituted with one or more halogen, C₁₋₆alkyl, amino, hydroxy, C₁₋₆alkoxyl or aryl.

Ar² represents an aryl group substituted with none, one or more halogen, C₁₋₆alkyl, amino, hydroxy, C₁₋₆alkoxyl or aryl; a hetero aryl, or a heterocyclic group optionally substituted with one or more halogen, C₁₋₆alkyl, amino, hydroxy, C₁₋₆alkoxyl or aryl.

20. A method according to claim 19 wherein said condition is selected from the group consisting of type 1 diabetes, type 2 diabetes, dyslipidemia, syndrome X, cardiovascular disease, atherosclerosis, hypercholesteremia, and obesity.

21. The method according to claim 20, wherein the effective amount of the compound is in the range of from about 0.05 to about 200mg/kg body weight per day.

22. The method according to claim 21, wherein the effective amount of the compound is in the range of from about 0.1 to about 100mg/kg body weight per day.

23. The method according to claim 22, where in the effective amount of the compound is in the range of from about 0.1 to about 50mg/kg body weight per day.

24. A method of treating or preventing a condition according to claim 19 comprising
5 administering to a subject in need thereof an effective amount of the compound in combination with at least one agent selected from the group consisting of a hypolipidemic agent, lipid-lowering agent, lipid modulating agent, antidiabetic agent, anti-obesity agent, antihypertensive agent, and a platelet aggregation inhibitor; which may be administered orally in the same dosage form, in a separate oral dosage form or by injection.

10 25. A method of treating or preventing a condition according to claim 24 wherein the hypolipidemic agent or lipid-lowering agent or lipid modulating agent is selected from the group consisting of at least one: MTP inhibitor, HMG CoA reductase inhibitor, squalene synthetase inhibitor, fibric acid derivative, ACAT inhibitor, lipoxxygenase inhibitor,
15 cholesterol absorption inhibitor, ileal Na⁺/bile acid cotransporter inhibitor, upregulator of LDL receptor activity, bile acid sequestrant, and nicotinic acid or a derivative thereof.

26. A method of treating or preventing a condition according to claim 24 wherein at least one antidiabetic agent is selected from the group consisting of an insulin secretagogue, an insulin
20 sensitizer, a biguanide, a sulfonyl urea, a glucosidase inhibitor, a PPAR γ partial agonist or antagonist, a thiazolidinedione, a P2 inhibitor, a dipeptidyl peptidase IV (DP4) inhibitor, a SGLT2 inhibitor, a meglitinide, insulin, and a glucagon-like peptide-1 (GLP-1).

27. A method of treating or preventing a condition according to claim 24 wherein at least one
25 agent is selected from the group consisting of an anti-obesity agent, a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake inhibitor, a P2 inhibitor, a thyroid receptor agonist, and an anorectic agent.

28. A method of treating or preventing a condition according to claim 24 wherein at least one
30 antihypertensive agent agent is selected from the group consisting of an ACE inhibitor, an

angiotensin II receptor antagonist, an NEP/ACE inhibitor, a calcium channel blocker, a β -adrenergic blocker and a diuretic.

* * *